

SEQUENCE LISTING

<110> Beamer, Les Entre
Eisenberg, David
Carroll, Stephen F.

<120> BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN:
 CRYSTALLIZATION, X-RAY DIFFRACTION, THREE-DIMENSIONAL
 STRUCTURE DETERMINATION, RATIONAL DRUG DESIGN AND
 MOLECULAR MODELING OF RELATED PROTEINS

<130> 11034US02

<140> 09/446,415

<141> 2000-07-19

<150> 08/879,565

<151> 1997-06-20

<160> 12

<170> PatentIn Ver. 2.1

<210> 1

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<212> DNA

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<223> "rBPI"

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-25

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Pro Cys Asn Ala Pro Arg Trp Val Ser Leu Met Val Leu Val Ala Ile
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Gly Thr Ala Val Thr Ala Ala Val Asn Pro Gly Val Val Arg Ile
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30 35 40

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													ggc Gly 120		486
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_												_	aac Asn	-	630
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													aac Asn		822
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													aac Asn		918
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gat gac atg Asp Asp Met			Ser									1014
ttt gga acc Phe Gly Thr 300	Phe Leu			_	_	_						1062
ata cag atc Ile Gln Ile 315	_	_			_			_			_	1110
ccc acc ggc Pro Thr Gly 330				_		_	_	_	_		_	1158
gtc ctc ccc Val Leu Pro												1206
aca act ggt Thr Thr Gly	_		Ser	_						_		1254
gag ctc aag Glu Leu Lys 380	Leu Asp											1302
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ccc att ctt Pro Ile Leu 410												1398
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<223> "rBPI"

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Asn Pro Gly Val Val Arg Ile Ser Gln Lys Gly Leu Asp Tyr Ala
5 10 15

Ser Gln Gln Gly Thr Ala Ala Leu Gln Lys Glu Leu Lys Arg Ile Lys 20 25 30

Ile Pro Asp Tyr Ser Asp Ser Phe Lys Ile Lys His Leu Gly Lys Gly 35 40 45

His Tyr Ser Phe Tyr Ser Met Asp Ile Arg Glu Phe Gln Leu Pro Ser 50 55 60 65

Ser Gln Ile Ser Met Val Pro Asn Val Gly Leu Lys Phe Ser Ile Ser 70 75 80

Asn Ala Asn Ile Lys Ile Ser Gly Lys Trp Lys Ala Gln Lys Arg Phe 85 90 95

Leu Lys Met Ser Gly Asn Phe Asp Leu Ser Ile Glu Gly Met Ser Ile
100 105 110

Ser Ala Asp Leu Lys Leu Gly Ser Asn Pro Thr Ser Gly Lys Pro Thr 115 120 125

Ile Thr Cys Ser Ser Cys Ser Ser His Ile Asn Ser Val His Val His 130 145

Ile Ser Lys Ser Lys Val Gly Trp Leu Ile Gln Leu Phe His Lys Lys
150 155 160

Ile Glu Ser Ala Leu Arg Asn Lys Met Asn Ser Gln Val Cys Glu Lys 165 170 175

Val Thr Asn Ser Val Ser Ser Lys Leu Gln Pro Tyr Phe Gln Thr Leu 180 185 190

Pro Val Met Thr Lys Ile Asp Ser Val Ala Gly Ile Asn Tyr Gly Leu 195 200 205

Val Ala Pro Pro Ala Thr Thr Ala Glu Thr Leu Asp Val Gln Met Lys 210 225 220

Gly Glu Phe Tyr Ser Glu Asn His His Asn Pro Pro Pro Phe Ala Pro
230 235 240

Pro Val Met Glu Phe Pro Ala Ala His Asp Arg Met Val Tyr Leu Gly 245 250 255

Leu Ser Asp Tyr Phe Phe Asn Thr Ala Gly Leu Val Tyr Gln Glu Ala 260 265 270

Gly Val Leu Lys Met Thr Leu Arg Asp Asp Met Ile Pro Lys Glu Ser 275 280 285

Lys Phe Arg Leu Thr Thr Lys Phe Phe Gly Thr Phe Leu Pro Glu Val 290 295 300 305

Ala Lys Lys Phe Pro Asn Met Lys Ile Gln Ile His Val Ser Ala Ser 310 315 320

Thr Pro Pro His Leu Ser Val Gln Pro Thr Gly Leu Thr Phe Tyr Pro 325 330 335

Ala Val Asp Val Gln Ala Phe Ala Val Leu Pro Asn Ser Ser Leu Ala 340 345 350

Ser Leu Phe Leu Ile Gly Met His Thr Thr Gly Ser Met Glu Val Ser 355 360 365

Ala Glu Ser Asn Arg Leu Val Gly Glu Leu Lys Leu Asp Arg Leu Leu 370 380 385

Leu Glu Leu Lys His Ser Asn Ile Gly Pro Phe Pro Val Glu Leu Leu 390 395 400

Gln Asp Ile Met Asn Tyr Ile Val Pro Ile Leu Val Leu Pro Arg Val 405 410 415

Asn Glu Lys Leu Gln Lys Gly Phe Pro Leu Pro Thr Pro Ala Arg Val 420 425 430

Gln Leu Tyr Asn Val Val Leu Gln Pro His Gln Asn Phe Leu Leu Phe 435 440 445

Gly Ala Asp Val Val Tyr Lys 450 455

<210> 3

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<213> Human

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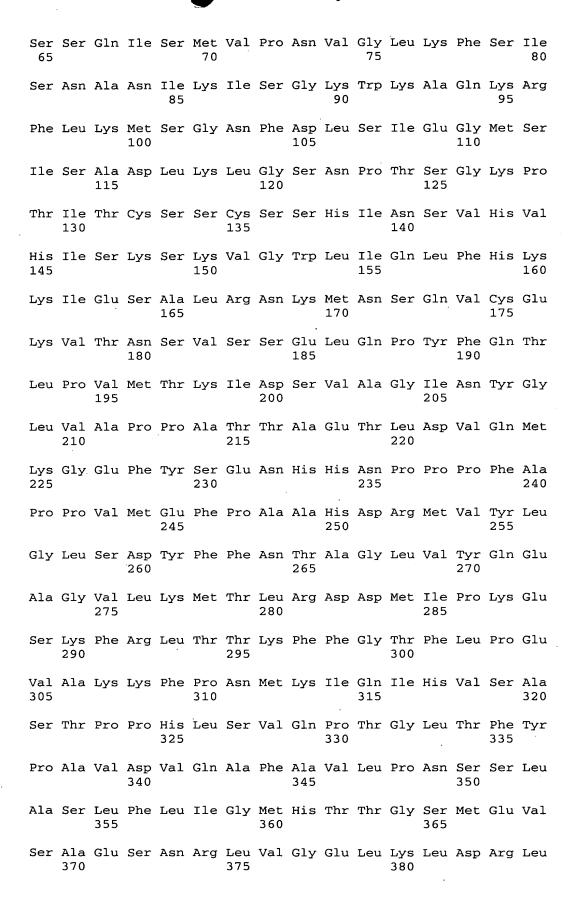
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Ala Ser Gln Gln Gly Thr Ala Ala Leu Gln Lys Glu Leu Lys Arg Ile 20 25 30

Lys Ile Pro Asp Tyr Ser Asp Ser Phe Lys Ile Lys His Leu Gly Lys 35 40 45

Gly His Tyr Ser Phe Tyr Ser Met Asp Ile Arg Glu Phe Gln Leu Pro 50 55 60



Leu Leu Glu Leu Lys His Ser Asn Ile Gly Pro Phe Pro Val Glu Leu 385 390 395 400

Leu Gln Asp Ile Met Asn Tyr Ile Val Pro Ile Leu Val Leu Pro Arg 405 410 415

Val Asn Glu Lys Leu Gln Lys Gly Phe Pro Leu Pro Thr Pro Ala Arg 420 425 430

Val Gln Leu Tyr Asn Val Val Leu Gln Pro His Gln Asn Phe Leu Leu 435 440 445

Phe Gly Ala Asp Val Val Tyr Lys 450 455

<210> 4

<211> 456

<212> PRT

<213> Human

<220>

<223> lipopolysaccharide binding protein (LBP) (Figure
5)

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Ala Asn Pro Gly Leu Val Ala Arg Ile Thr Asp Lys Gly Leu Gln Tyr 1 5 10 15

Ala Ala Glu Glu Leu Leu Ala Leu Glu Ser Glu Leu Leu Arg Ile 20 25 . 30

Thr Leu Pro Asp Phe Thr Gly Asp Leu Arg Ile Pro His Val Gly Arg 35 40 45

Gly Arg Tyr Glu Phe His Ser Leu Asn Ile His Ser Cys Glu Leu Leu 50 55 60

His Ser Ala Leu Arg Pro Val Pro Gly Gln Gly Leu Ser Leu Ser Ile 65 70 75 80

Ser Asp Ser Ser Ile Arg Val Gln Gly Arg Trp Lys Val Arg Lys Ser 85 90 95

Phe Phe Lys Leu Gln Gly Ser Phe Asp Val Ser Val Lys Gly Ile Ser 100 105 110

Ile Ser Val Asn Leu Leu Gly Ser Glu Ser Ser Gly Arg Pro Thr 115 120 125

Val Thr Ala Ser Ser Cys Ser Ser Asp Ile Ala Asp Val Glu Val Asp 130 . 135 140

Met Ser Gly Asp Leu Gly Trp Leu Leu Asn Leu Phe His Asn Gln Ile 145 150 155 160

Glu Ser Lys Phe Gln Lys Val Leu Glu Ser Arg Ile Cys Glu Met Ile 165 170 175

Gln Lys Ser Val Ser Ser Asp Leu Gln Pro Tyr Leu Gln Thr Leu Pro 180 185 190

220

Val Thr Thr Glu Ile Asp Ser Phe Ala Asp Ile Asp Tyr Ser Leu Val 195 200 205

Glu Ala Pro Arg Ala Thr Ala Gln Met Leu Glu Val Met Phe Lys Gly

Glu Ile Phe His Arg Asn His Arg Ser Pro Val Thr Leu Leu Ala Ala 225 230 235 240

215

Val Met Ser Leu Pro Glu Glu His Asn Lys Met Val Tyr Phe Ala Ile 245 250 255

Ser Asp Tyr Val Phe Asn Thr Ala Ser Leu Val Tyr His Glu Glu Gly 260 265 270

Tyr Leu Asn Phe Ser Ile Thr Asp Asp Met Ile Pro Pro Asp Ser Asn 275 280 285

Ile Arg Leu Thr Thr Lys Ser Phe Arg Pro Phe Val Pro Arg Leu Ala 290 295 300

Arg Leu Tyr Pro Asn Met Asn Leu Glu Leu Gln Gly Ser Val Pro Ser 305 310 315 320

Ala Pro Leu Leu Asn Phe Ser Pro Gly Asn Leu Ser Val Asp Pro Tyr 325 330 335

Met Glu Ile Asp Ala Phe Val Leu Leu Pro Ser Ser Lys Glu Pro 340 345 350

Val Phe Arg Leu Ser Val Ala Thr Asn Val Ser Ala Thr Leu Thr Phe 355 360 365

Asn Thr Ser Lys Ile Thr Gly Phe Leu Lys Pro Gly Lys Val Lys Val 370 380

Glu Leu Lys Glu Ser Lys Val Gly Leu Phe Asn Ala Glu Leu Leu Glu 385 390 395 400

Ala Leu Leu Asn Tyr Tyr Ile Leu Asn Thr Phe Tyr Pro Lys Phe Asn 405 410 415

Asp Lys Leu Ala Glu Gly Phe Pro Leu Pro Leu Lys Arg Val Gln 420 425 430

Leu Tyr Asp Leu Gly Leu Gln Ile His Lys Asp Phe Leu Phe Leu Gly 435 440 445

Ala Asn Val Gln Tyr Met Arg Val 450 455

<210> 5

<211> 476

<212> PRT

<213> Human

<220>

<223> phospholipid transfer protein (PLTP) (Figure 5)

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Thr Tyr Phe Gly Ser Ile Val Leu Leu Ser Pro Ala Val Ile Asp Ser 290

Pro Leu Lys Leu Glu Leu Arg Val Leu Ala Pro Pro Arg Cys Thr Ile 305

310

320

Lys Pro Ser Gly Thr Thr Ile Ser Val Thr Ala Ser Val Thr Ile Ala 325 330 335

Leu Val Pro Pro Asp Gln Pro Glu Val Gln Leu Ser Ser Met Thr Met 340 345 350

Asp Ala Arg Leu Ser Ala Lys Met Ala Leu Arg Gly Lys Ala Leu Arg 355 360 365

Thr Gln Leu Asp Leu Arg Arg Phe Arg Ile Tyr Ser Asn His Ser Ala 370 375 380

Leu Glu Ser Leu Ala Leu Ile Pro Leu Gln Ala Pro Leu Lys Thr Met 385 390 395 400

Leu Gln Ile Gly Val Met Pro Met Leu Asn Glu Arg Thr Trp Arg Gly 405 410 415

Val Gln Ile Pro Leu Pro Glu Gly Ile Asn Phe Val His Glu Val Val 420 425 430

Thr Asn His Ala Gly Phe Leu Thr Ile Gly Ala Asp Leu His Phe Ala 435 440 445

Lys Gly Leu Arg Glu Val Ile Glu Lys Asn Arg Pro Ala Asp Val Arg 450 455 460

Ala Ser Thr Ala Pro Thr Pro Ser Thr Ala Ala Val 465 470 475

<210> 6

<211> 470

<212> PRT

<213> Human

<220>

<223> cholesteryl ester transfer protein (CETP) (Figure
5)

<400> 6

His Glu Ala Gly Ile Val Cys Arg Ile Thr Lys Pro Ala Leu Leu Val
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Ser Tyr Pro Asp Ile Thr Gly Glu Lys Ala Met Met Leu Leu Gly Gln 35 40 45

Val Lys Tyr Gly Leu His Asn Ile Gln Ile Ser His Leu Ser Ile Ala 50 55 60

Ser Ser Gln Val Glu Leu Val Glu Ala Lys Ser Ile Asp Val Ser Ile 65 70 75 80

Gln Asn Val Ser Val Val Phe Lys Gly Thr Leu Lys Tyr Gly Tyr Thr 85 90 95

Thr Ala Trp Trp Leu Gly Ile Asp Gln Ser Ile Asp Phe Glu Ile Asp 100 105 110

Ser	Ala	Ile 115	Asp	Leu	Gln.	Ile	Asn 120	Thr	Gln	Leu	Thr	Cys 125	Asp	Ser	Gly
Arg	Val 130	Arg	Thr	Asp	Ala	Pro 135	Asp	Cys	Tyr	Leu	Ser 140	Phe	His	Lys	Leu
Leu 145	Leu	His	Leu	Gln	Gly 150	Glu	Arg	Glu	Pro	Gly 155	Trp	Ile	Lys	Gln	Leu 160
Phe	Thr	Asn	Phe	Ile 165	Ser	Phe	Thr	Leu	Lys 170	Leu	Val	Leu	Lys	Gly 175	Gln
Ile	Cys	Lys	Glu 180	Ile	Asn	Val	Ile	Ser 185	Asn	Ile	Met	Ala	Asp 190	Phe	Val
Gln	Thr	Arg 195	Ala	Ala	Ser	Ile	Leu 200	Ser	Asp	Gly	Asp	Ile 205	Gly	Val	Asp
Ile	Ser 210	Leu	Thr	Gly	Asp	Pro 215	Val	Ile	Thr	Ala	Ser 220	Tyr	Leu	Glu	Ser
His 225	His	Lys	Gly	His	Phe 230	Ile	Tyr	Lys	Asn	Val 235	Ser	Glu	Asp	Leu	Pro 240
Leu	Pro	Thr	Phe	Ser 245	Pro	Thr	Leu	Leu	Gly 250	Asp	Ser	Arg	Met	Leu 255	Tyr
Phe	Trp	Phe	Ser 260	Glu	Arg	Val	Phe	His 265	Ser	Leu	Ala	Lys	Val 270	Ala	Phe
Gln	Asp	Gly 275	Arg	Leu	Met	Leu	Ser 280	Leu	Met	Gly	Asp	Glu 285	Phe	Lys	Ala
		275	_				280					285		Lys	
Val	Leu 290	275 Glu	Thr	Trp	Gly	Phe 295	280 Asn	Thr	Asn	Gln	Glu 300	285 Ile	Phe		Glu
Val Val 305	Leu 290 Val	275 Glu Gly	Thr	Trp Phe	Gly Pro 310	Phe 295 Ser	280 Asn Gln	Thr Ala	Asn Gln	Gln Val 315	Glu 300 Thr	285 Ile Val	Phe His	Gln	Glu Leu 320
Val 305 Lys	Leu 290 Val Met	275 Glu Gly Pro	Thr Gly Lys	Trp Phe Ile 325	Gly Pro 310 Ser	Phe 295 Ser Cys	280 Asn Gln	Thr Ala Asn	Asn Gln Lys 330	Gln Val 315 Gly	Glu 300 Thr	285 Ile Val	Phe His Val	Gln Cys Asn	Glu Leu 320 Ser
Val Val 305 Lys Ser	Leu 290 Val Met	275 Glu Gly Pro	Thr Gly Lys Val	Trp Phe Ile 325	Gly Pro 310 Ser	Phe 295 Ser Cys Leu	280 Asn Gln Gln Phe	Thr Ala Asn Pro 345	Asn Gln Lys 330 Arg	Gln Val 315 Gly Pro	Glu 300 Thr Val	285 Ile Val Val	Phe His Val Gln 350	Gln Cys Asn 335	Glu Leu 320 Ser
Val 305 Lys Ser	Leu 290 Val Met Val	275 Glu Gly Pro Met Tyr 355	Thr Gly Lys Val 340	Trp Phe Ile 325 Lys Phe	Gly Pro 310 Ser Phe Glu	Phe 295 Ser Cys Leu Glu	280 Asn Gln Gln Phe Asp 360	Thr Ala Asn Pro 345	Asn Gln Lys 330 Arg	Gln Val 315 Gly Pro	Glu 300 Thr Val Asp	285 Ile Val Val Gln Val 365	Phe His Val Gln 350	Gln Cys Asn 335 His	Glu Leu 320 Ser Ser
Val 305 Lys Ser Val	Leu 290 Val Met Val Ala Ser 370	275 Glu Gly Pro Met Tyr 355 Lys	Thr Gly Lys Val 340 Thr	Trp Phe Ile 325 Lys Phe	Gly Pro 310 Ser Phe Glu Leu	Phe 295 Ser Cys Leu Glu Phe 375	280 Asn Gln Gln Phe Asp 360 Leu	Thr Ala Asn Pro 345 Ile Ser	Asn Gln Lys 330 Arg Val	Gln Val 315 Gly Pro Thr	Glu 300 Thr Val Asp Thr	285 Ile Val Val Gln Val 365 Phe	Phe His Val Gln 350 Gln	Gln Cys Asn 335 His	Glu Leu 320 Ser Ser
Val 305 Lys Ser Val Tyr Pro 385	Leu 290 Val Met Val Ala Ser 370 Lys	275 Glu Gly Pro Met Tyr 355 Lys	Thr Gly Lys Val 340 Thr Lys	Trp Phe Ile 325 Lys Phe Lys	Gly Pro 310 Ser Phe Glu Leu Asn 390	Phe 295 Ser Cys Leu Glu Phe 375 Leu	280 Asn Gln Gln Phe Asp 360 Leu Thr	Thr Ala Asn Pro 345 Ile Ser Glu	Asn Gln Lys 330 Arg Val Leu Ser	Gln Val 315 Gly Pro Thr Leu Ser 395	Glu 300 Thr Val Asp Thr Asp 380 Ser	285 Ile Val Val Gln Val 365 Phe Glu	Phe His Val Gln 350 Gln Gln Ser	Gln Cys Asn 335 His Ala Ile	Glu Leu 320 Ser Ser Thr

Ser Leu Phe Asp Ile Ile Asn Pro Glu Ile Ile Thr Arg Asp Gly Phe 435 440 Leu Leu Gln Met Asp Phe Gly Phe Pro Glu His Leu Leu Val Asp 455 460 Phe Leu Gln Ser Leu Ser 465 470 <210> 7 <211> 42 <212> DNA <213> Human <220> <223> oligonucleotide from XcmI site to SphI site within BPI gene (encoding residues 348-361) containing the codon TCC for the serine at amino acid position 351 cccaactcct ccctggcttc cctcttcctg attggcatgc ac 42 <210> 8 <211> 42 <212> DNA <213> Human <220> <223> Oligonucleotide complementary to SEQ ID NO:5 <400> 8 42 gggttcagga gggaccgaag ggagaaggac taaccgtacg tg <210> 9 <211> 14 <212> PRT <213> Human <220> <223> "wild type" amino acid sequence of residues 348-361 in BPI Pro Asn Ser Ser Leu Ala Ser Leu Phe Leu Ile Gly Met His <210> 10 <211> 42 <212> DNA <213> Human <220> <223> oligonucleotide from XcmI site to SphI site within the BPI gene (encoding residues 348-361) containing the codon GCC for alanine at amino acid

position 351

<400> 10 cccaactccg ccctggcttc cctcttcctg attggcatgc ac	42
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<220> <223> Oligonucleotide complementary to SEQ ID NO:8	
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<220> <223> "nonglycosylated" amino acid sequence of residues 348-361 in BPI	
<400> 12 Pro Asn Ser Ala Leu Ala Ser Leu Phe Leu Ile Gly Met His 1 5 10	